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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,175	DALY ET AL.	
	Examiner	Art Unit	
	Yong D. Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *5,7-11,13-24 and 29-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,12,25-28 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/4/03 & 03/27/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.00

DETAILED ACTION

This application is a continuation of PCT/US00/26504.

Claims 1-41 are pending. Claims 5, 7-11, 13-24 and 29-40 are withdrawn. Claims 1-4, 6, 12, 25-28 and 41 are under consideration.

Election/Restrictions

Applicant's election with traverse of Group I (*D. radiodurans* expressing proteins encoded by the *mer* operon) with a further election of detoxifying heavy metals in the reply filed on June 22, 2005 is acknowledged. The traversal is on the ground(s) that there would not be an undue burden in searching all the radiation resistant bacterium claimed or all detoxifying genes because the search is not extensive and would identify relevant art. This is not found persuasive because the search for all the claimed bacterium expressing patentably distinct proteins requires a separate search and therefore, a search for all detoxifying genes is not co-extensive and would impose a burden to the Examiner.

The traversal is on the ground(s) that the restriction should not be limited to a single bacterium expressing a specific heterologous protein because it would unduly restrict the claims to one particular detoxifying agent and election of a particular detoxifying protein should be withdrawn. This is not found persuasive because a special technical feature that links all the heterologous proteins recited in claim 12, as discussed in the previous Restriction Requirement. Each heterologous protein has a distinct structure and function.

The traversal is also on the ground(s) that the reference of Lange et al. used to demonstrate a lack of special technical feature as it does not define a contribution over the art was published within a year of the instant application's priority date and therefore, the reference is not available as prior art rendering the lack of unity of invention invalid. This is not found persuasive because the inventive entity of the reference is different from that of the instant application and Lange et al. was published before the priority date of the instant application. Therefore, the reference is a bona fide prior art document.

The requirement is still deemed proper and is therefore made **FINAL**.

Claims 5, 7-11, 13-24 and 29-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on September 7, 2004.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on February 4, 2003 and March 27, 2002 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, page 2 of the specification for example. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

Claims 3-4, 12 and 41 are objected to because the claim is drawn to non-elected products, such as *Enterococcus, Alcaligenes*, radionuclides, organic compounds, tol regions, *D. radiopugnans*.

Claim 12 is objected because of the following informalities: Claim 12 is objected for improper grammar. The claim should recite "proteins encoded by", in line 3. Appropriate correction is required.

Claims 25 and 41 are objected to because said claims depend from non-elected claims.

Claims 27-28 are objected to because of the following informalities: Claims 27-28 are objected for improper grammar. The claims recite the word "if" instead of "is" in line 1. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 and claims 2-4, 6, 25-28 and 41 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the term "radiation". The metes and bounds of the term in the context of the above claim are not clear to the Examiner. It is not clear to the Examiner what types of radiations are encompassed, i.e. ionizing, non-ioninzing, radioactive, non-radioactive, ultraviolet, infrared, etc. A perusal of the specification did not provide the Examiner with a specific definition of the above term. Examiner requests clarification.

Claim 1 and claims 2-4, 6, 25-28 and 41 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the phrase "engineered to detoxify at least one toxin". The metes and bounds of the phrase in the context of the above claim are not clear to the Examiner. It is not clear as to what type of "toxins" are encompassed in the above phrase. A perusal of the specification did not provide the Examiner with a specific definition of the above phrase. Examiner requests clarification.

Claim 4 and claim 6 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites the phrase "organic compounds". The metes and bounds of the phrase in the context of the above claim are not clear to the Examiner. It is not clear as to what type of "organic compounds" are encompassed in the above phrase. A perusal of the specification did not provide the Examiner with a specific definition of the above phrase. Examiner requests clarification.

Claims 27-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 27-28 recite the phrase "formulated for controlled release". The metes and bounds of the phrase in the context of the above claim are not clear to the Examiner. A perusal of the specification did not provide the Examiner with a specific definition for the above phrase. Therefore, it is not clear to the Examiner what is "controlled release", the bacterium, proteins encoded by the *mer* operon, film forming agent or a nutrient agent.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4, 6, 12, 25-28 and 41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-2, 4, 6 and 41 are drawn to radiation resistant bacterium engineered to detoxify the recited toxins and has the properties recited in claim 2. Claims 12 and 25-28 are drawn to a radiation resistant bacterium engineered to express heterologous proteins encoded by the *mer* operon and a bioremediation composition comprising said bacterium and a film forming or a nutrient agent, wherein the composition is formulated for controlled release. Therefore, these claims are drawn to any or all bacteria having any structure, wherein the bacterium detoxifies any toxins, radionuclides, heavy metals and organic compounds. The specification only discloses a single species *D. radiodurans* transformed to express proteins encoded by the *mer* operon isolated from *E. coli,* wherein the transformed bacterium detoxifies a single heavy metal, mercury. Therefore, the specification fails to describe a representative number of species comprising a genus of bacteria which is resistant to radiation and at the same time able to detoxify a toxin.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 1-2, 4, 6, 12, 25-28 and 41.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-4, 6, 12, 28-28 and 41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a radiation resistant *D. radiodurans* transformed to express proteins encoded by the *mer* operon isolated from *E.coli*, such that the transformed bacteria is radiation resistant (ionizing radiation) and detoxifies mercury, does not reasonably provide enablement for any or all bacterium, including any or all mutants, variants, and recombinants engineered to express proteins encoded by a mer operon from any source, or engineered by any or all types of techniques to detoxify any or all toxins, radionuclides, heavy metals or organic compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 1-4, 6 and 41 are drawn to any or all bacterium, including any or all mutants, variants, and recombinants engineered by any or all types of techniques to detoxify any or all toxins, radionuclides, heavy metals or organic compound. Claims 12 and 25-28 are drawn to a radiation resistant bacterium engineered to express heterologous proteins encoded by the *mer* operon and a bioremediation composition comprising said bacterium and a film forming agent or a nutrient agent, wherein the composition is formulated for controlled release. Therefore, these claims are drawn to any or all bacteria engineered using any or all techniques, wherein said bacterium detoxifies any toxins, radionuclides, heavy metals and organic compounds.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of bacterium engineered using any or all techniques encompassed by the claims to detoxify any or all toxins. The scope of the claims is also not commensurate with the enablement provided by the disclosure with regard to the extremely large number of bacteria engineered to express proteins encoded by a *mer* operon from any source, as encompassed by the claims. Since bacteria are a highly diverse group of organisms and since each species behaves differently, predictability of which modifications can be tolerated by any or all bacteria that results in a radiation resistant bacteria that detoxifies heavy metals requires a knowledge and guidance with regard to which bacteria, mer operon and/or engineering techniques to use and how tolerant the bacteria are to such modifications. While microbiological techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple species or multiple modifications as

encompassed by the instant claims, the specific bacterial species in which modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given bacteria to diminish with each further and additional modification.

Therefore, it would require undue experimentation of the skilled artisan to make any bacterium using any techniques or any bacterium expressing proteins encoded by any or all *mer* operon from any source, wherein the bacteria has the properties recited in claims 2 and 4. The specification is limited to the teaching of a modified *D. radiodurans,* which is naturally resistant to radiation, modified by transformation to express proteins encoded by the mer operon isolated from *E. coli,* wherein the transformed bacterium detoxifies mercury. In view of the great breadth of the claims, amount of experimentation required to make the claimed bacterium, the lack of guidance, working examples, and unpredictability of the art in predicting which techniques to engineer any bacterium to detoxify any toxin or which mer operon to use to transform any bacteria, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the method encompassed by the claims.

The specification does not support the broad scope of the claims which encompass any or all bacterium, including any or all mutants, variants, and recombinants engineered to express proteins encoded by a mer operon from any source or engineered by any or all types of techniques to detoxify any or all toxins,

radionuclides, heavy metals or organic compound because the specification does not establish: (A) bacteria which may be modified without that results in a radiation resistant bacteria that also detoxifies heavy metals; (B) microbiological techniques which may be used to modify any or all bacteria that results in a in a radiation resistant bacteria that also detoxifies heavy metals; (C) a rational and predictable scheme for modifying any bacteria using any techniques with an expectation of obtaining the desired biological function; (D) the general tolerance of any or all bacterium to modification by any or all techniques and extent of such tolerance; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any or all bacterium, including any or all mutants, variants, and recombinants engineered to express proteins encoded by a *mer* operon from any source or engineered by any or all types of techniques to detoxify any or all toxins, radionuclides, heavy metals or organic compound. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of which bacteria to modify and which engineering techniques to use is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-4, 12, 25 and 41 are rejected under 35 U.S.C. 102(a) as being anticipated by Lange et al.

Claims 1-4, 12, 25 and 41 are drawn to radiation resistant *D. radiodurans* engineered to express proteins encoded by *Psudomonoas Tol* region, wherein the bacterium grows in the presence of continuous radiation of about 60 Gy/hour and detoxifies toxins, such as organic compounds and bioremediation composition comprising said bacterium.

Lange et al. (form PTO-1449) discloses a radiation resistant *D. radiodurans* engineered to express proteins encoded by *Psudomonoas Tol* region, wherein the bacterium grows in the presence of continuous radiation of about 60 Gy/hour and detoxifies toxins, such as organic compounds (page 930 and 932). Lange et al. also disclose a bioremediation composition comprising said bacterium (abstract). Therefore, the reference of Lange et al. anticipates claims 1-4, 12, 25 and 41.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 6, 12, 25 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kurabayashi et al. and Carroll et al.

Claims 1-4, 6, 12, 25 and 41 are drawn to radiation resistant *D. radiodurans* engineered to express proteins encoded by a *mer* operon, wherein the bacterium grows in the presence of continuous radiation of about 60 Gy/hour and detoxifies toxins, such as heavy metals.

Kurabayashi et al. (form PTO-892) discloses a plasmid comprising a *mer* operon and bacteria transformed with said plasmid (page 1187). Kurabayashi et al. teaches

that the transformed bacteria converts toxic mercury (Hg^{2+}) to the less toxic elemental form, Hg^0 and that the bacteria can be used to improve mercury-contaminated soil (pages 1187-1188).

The difference between the reference of Kurabayashi et al. and the instant invention is that Kurabayashi et al. does not teach a radiation resistant *D. radiodurans* expressing proteins encoded by a *mer* operon.

Carroll et al. (form PTO-892) discloses that radiation resistant *D. radiodurans* is naturally transformable and is amenable to genetic manipulation (page 130 and Table 1 on page 131). Carroll et al. teaches how to express heterologous proteins in *D. radiodurans*, wherein the resulting bacterium can grow in the presence of 60 Gy/hour (page 133, Figure 5). One having ordinary skill in the art would have recognized the advantage of making a bacterium having resistance to both radiation and mercury, for its application in detoxifying mercury contaminated radioactive wastes.

Therefore, combining the teachings of the above two references, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to engineer a *D. radiodurans* of Carroll to express proteins encoded by a *mer* operon taught by Kurababyashi et al. One of ordinary skill in the art would have been motivated to make a bacterium having resistance to both radiation and mercury, for its application in detoxifying mercury contaminated radioactive wastes. One of ordinary skill in the art would have had a reasonable expectation of success in expressing proteins encoded by the *mer* operon in *D. radiodurans* since Kurabayashi et al. teaches

plasmids comprising said operon and Carroll et al. teaches how to transfom *D. radiodurans* with foreign polynucleotides.

Therefore, Kurabayashi et al. and Carroll et al. render claims 1-4, 6, 12, 25 and 41 *prima facie* obvious to those skilled in the art.

Claims 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kurabayashi et al. and Carroll et al. as applied to claims 1-4, 6, 12, 25 and 41 above, and further in view of Lin et al.

Claims 25-28 are drawn to a bioremediation composition comprising a radiation resistant *D. radiodurans* engineered to detoxify toxins, film forming agents and a nutrient agent, wherein the composition is formulated for controlled release.

Kurabayashi et al and Carroll et al. in combination teach a radiation resistant *D. radiodurans* engineered to detoxify toxins, as discussed above.

The difference between the combined references of Kurabayashi et al. and Carroll et al. and the instant invention is that a bioremediation composition comprising a radiation resistant *D. radiodurans* engineered to detoxify toxins is not taught.

Lin et al. (WO 95/08513 – form PTO-892) discloses a bioremediation composition comprising bacteria, film forming agents and nutrient agents, wherein the composition is formulated for controlled release (abstract and pages 1-2). Lin et al. teaches that said composition formulated for controlled release with film forming agents and nutrient agents enhances biodegradation of toxic compounds (page 5).

Therefore, combining the teachings of the above three references, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to formulate a *D. radiodurans* transformed with a *mer* operon for controlled release by using film forming agents and nutrient agent. One of ordinary skill in the art would have been motivated to make such a composition in order to enhance biodegradation of mercury contaminated radioactive wastes. One of ordinary skill in the art would have had a reasonable expectation of success in making such a composition since Lin et al. teaches how to formulate bioremediation compositions comprising bacteria for controlled release using filming and nutrient agents and Kurabayashi et al. and Carroll et al. in combination teaches a radiation resistant *D. radiodurans* that detoxifies mercury.

Therefore, Kurabayashi et al., Carroll et al. and Lin et al. render claims 25-28 *prima facie* obvious to those skilled in the art.

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner

Manjunath Rao
Primary Patent Examiner 1652